Toxic organic materials in the environment

TERENCE CARTER, JOHN BUTCHER AND COLIN CREASER

Controversies over the environmental impact of industrial processes and the effects of discharges and emissions highlight the importance of analytical techniques for the detection and measurement of toxic materials in the environment. The Harwell Laboratory is one of Europe's leading centres for analyses in connection with such environmental issues, and its expertise in organic, inorganic and environmental analysis is provided through the Physico-Chemical Measurements Unit (PCMU).

PCMU's array of facilities has recently been extended with the acquisition of a new gas chromatograph-mass spectrometer (GC-MS). The instrument (a Finnigan 1020B) complements the Unit's existing VG Analytical ZAB-1F high resolution mass spectrometer, and is intended particularly for the analysis of complex organic mixtures. Much of the work of PCMU is concerned with the identification of organics in environmental or occupational hygiene samples. Currently, for example, its efforts are being applied to the measurement of a range of potentially harmful chlorinated organic materials which have caused public concern in recent years. Figure 1 shows part of the chromatogram obtained from an extract of a soil sample from the Eglin USAF base in Florida known to have been contaminated with Agent Orange (a mixture of the herbicides 2,4-D and 2,4,5-T, used as a defoliant in the Vietnam War). The presence of the highly toxic 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in this sample is clearly identified from its mass spectrum (Fig 2), at a level of approximately 70μg/kg.[1] Another example concerns the measurement of polychlorinated biphenyls (PCBs), which have been used extensively, since their introduction in the early 1930s, as insulating media in electrical transformers and capacitors. Evidence for the harmful effects of PCBs prompted restrictions on their use in Britain in the early 1970s, which in turn led to prohibition of the further sale of PCBs in 1980.[2] The widespread contamination resulting from the manufacture and use of PCBs has given rise to the need for detecting these materials, at low levels, in a variety

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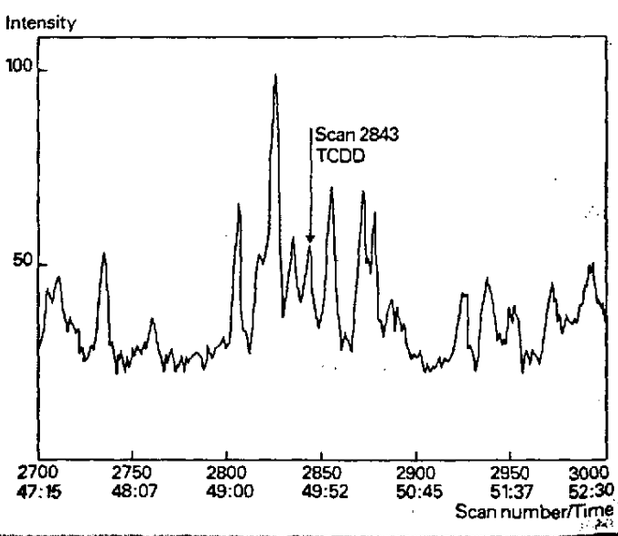
Fig 1 Part of chromatogram of soil extract, showing TCDD peak



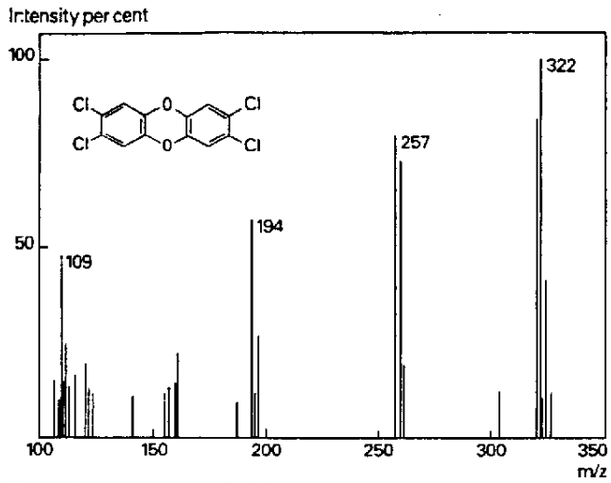


Fig 2 Mass spectrum of TCDD (scan 2843)

of environmental samples, including transformer fluids (from transformers previously filled with PCB), concrete, soil and blood. Several analytical techniques may be employed, including gas chromatography with electron capture detection (Fig 3) and GC-MS, the choice depending on the level of PCB to be measured and the specificity required. Typically, the levels encountered range from parts per billion (10^9) in blood to percent in concrete after a spill. Dielectric fluids in electrical equipment must contain less than 1000ppm in the UK[3] and less than 50ppm in the US in order not to be classified as PCBs.

PCMU's role in major multidisciplinary assessment and analysis programmes (which include the design of experiments, sampling, co-ordination of analytical measurements and interpretation of the results), is illustrated in a third example. Recently Harwell has concluded an investigation

Fig 3 Electron capture response for 500ppm Aroclor 1254 in mineral oil (dilute n-hexane solution)

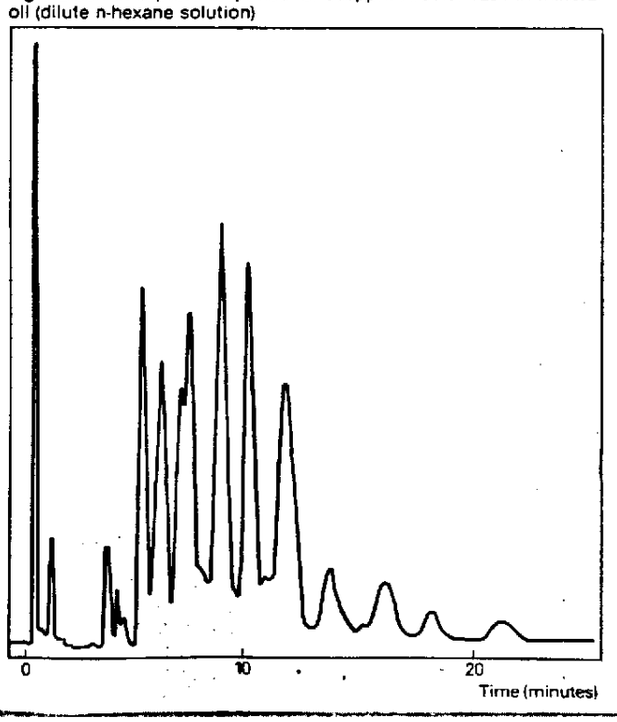


Fig 4 A catastrophic failure test

for the Electricity Council in connection with the development of a non-flammable dielectric and cooling fluid with a low toxicity profile for use in transformers. This new fluid is an alternative to the widely used BS 148 hydrocarbon oil, which, in the event of catastrophic failure, may give rise to a fireball which can endanger both life and property. The programme for assessing possible alternative fluids necessitated a series of large-scale destructive tests, leading ultimately to that of a full-scale sealed transformer. A unique and robust gas-sampling system was designed and built by the PCMU to collect any toxic vapours produced, and a number of such devices were arranged around a test cell at the time of a catastrophic failure (Fig 4). Sample collection pumps were activated individually by remote control, thereby permitting both spatial and time profiles of vapours to be measured. A variety of infrared spectrometric and chemical analyses were carred out 'on the spot', since many of the species of interest were labile. The large amount of analytical data resulting from the tests was used as the basis for a hazard assessment study by Harwell's Environmental Safety Group. A new transformer fluid, Elcool-NF, is now being marketed worldwide as the result of this work.

These examples illustrate the many organic environmental investigations which are carried out by the PCMU; others include medical and biological studies and industrial assessments. They emphasise the importance of the most accurate and reliable analyses in addressing environmental issues which are often surrounded by public controversy. These can only be carried out using the most sophisticated and sensitive analytical instruments, and often by using a combination of techniques. Since PCMU was set up in 1968, it has installed new instrumentation costing over £2.5M to maintain its role at the forefront of the analytical field.

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2 The Control of Pollution (supply and use of injurious substances) Regulations, HMSO, 1980 (SI No. 638)
3 Waste Management Paper No. 6: Polychlorinated Biphenyl (PCB) Wastes, UK Department of Environment

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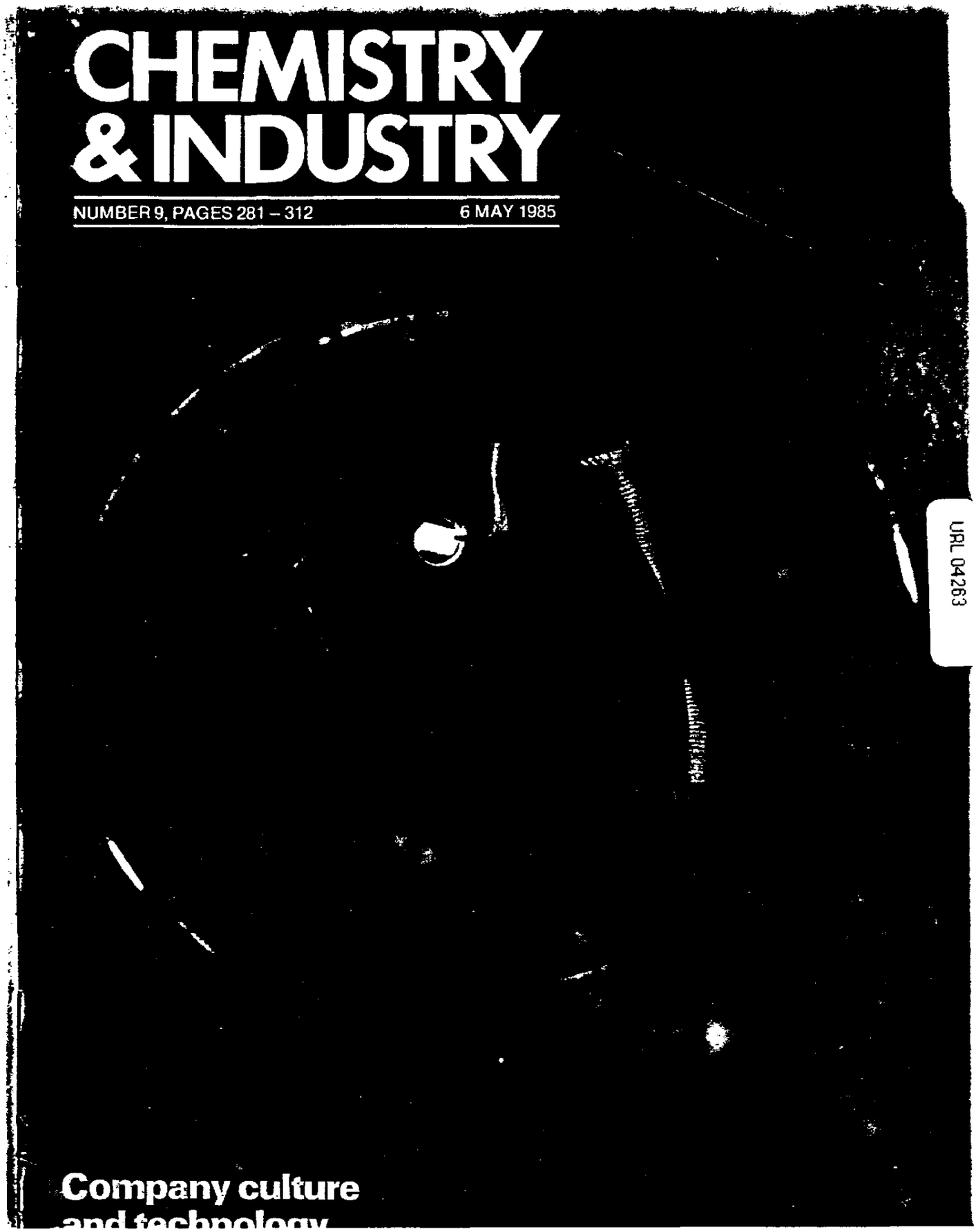

Company culture and technology

CANCER, POLLUTION AND THE WORKPLACE

A Special Report By:

AIHC The American Industrial Health Council

Cancer, pollution and the workplace

One of the most tragic aspects of cancer in America is that more of it could be prevented if only we applied our resources better.

Every dollar misspent, every laboratory hour misapplied represents a failure of priorities in the war against this deadly disease. That's why it's crucial that cancer prevention priorities be based only on sound data carefully interpreted by experts.

But in the last decade, too often that's not the way the public has set priorities. The assertion in the early 1970's that most causes of cancer are "in the environment" triggered a worldwide effort to identify and deal with those causes.

We looked for cancer causes in the physical environment--in the air, in water, virtually *everywhere* in the world around us. But too many of us overlooked the *personal environment*--what we put into our bodies. Maybe we didn't want to think about changing our lifestyle. Maybe it was a lot easier to lay most of the blame on "man-made chemicals" in the atmosphere generally, or in the workplace, or even in the home.

This was especially true in discussions of the American workplace. Wild "estimates" of on-the-job cancer hazards too often went unchallenged. Yet internationally-renowned epidemiologists (scientists who study the incidence and causes of disease) have known that the way we live--what we eat and drink, whether we smoke--has far more to do with cancer causation than workplace exposures. They contend that no more than 5% of cancer among Americans is the result of workplace exposure.

Of course, that's bad enough. We must deal with every cause of cancer. We are all concerned about even a single incidence of cancer resulting from an on-the-job exposure because it involves potentially preventable

human suffering and loss of life. That's why we've prepared this analysis – to tell you what is known about this vital issue and what we're doing about it.

Why is it so important that we know where to look for the sources of cancer?

A clear understanding of the probable sources of cancer allows research resources to be allocated effectively. As Dr. Harry Demopoulos, Associate Professor of Pathology, New York University Medical Center has said, "We cannot afford, not in monetary terms or in human terms, to spend another ten years and another billion dollars or more chasing the wrong culprit in cancer causation. There will be too many lives lost . . ."[1]

How do we know that lifestyle is so important in cancer causation?

Epidemiologists, including those from the World Health Organization's International Agency for Research on Cancer, have studied populations in many countries. These studies have compared the lifestyle and diets of the inhabitants with the kind of cancers that occur among them. They have found repeatedly that cancer patterns vary from country to country according to lifestyle factors.

For example, fat in the diet is suspected of playing an important role in cancer causation. The Japanese have a low-fat diet, and a significantly lower rate of colon and breast cancer than Americans. However, third generation descendants of Japanese immigrants to the U.S. have rates of colon and breast cancer similar to those of the American population as a whole.[2]

Copenhagen has a rate of colon cancer four times

greater than cities in Finland. Both populations have similar geographic and socio-economic conditions, but they have very different diets.[3]

On another front, many epidemiological studies have shown that smokers have a 10 times greater chance of getting lung cancer than non-smokers.

How much cancer is related to chemicals in the environment?

Since life is essentially a chemical process, all cancer might be said to be related to chemicals in the environment. However, cancer epidemiology experts, drawing on extensive studies of various populations, estimate that man-made chemicals may account for 1-5% of all cancer in the United States. Much of this 1-5% is apparently due to workplace exposure.

How can scientists be certain that man-made chemicals cause such a small proportion of cancer?

These estimates are derived by analyzing what is known about cancer occurrence. For example, studies show that if you exclude tobacco-related lung cancer, the incidence of cancer in non-industrial Geneva, Switzerland, is higher than in industrial England. And non-industrial San Francisco has a higher cancer incidence than industrial Pittsburgh.

Research in the United Kingdom has indicated that cancer incidence is more related to socio-economic class than it is to occupational exposure. There is little difference in overall cancer mortality between gas, coke and chemical workers and a standardized sample of all workers in the same social class.[4]

Dr. Demopoulos[5] has summarized generally-accepted

estimates of cancer causation based on mortality as follows:

. . . 35% are related to smoking and alcohol consumption.

. . . 45% are related to "disordered" nutrition, obesity, diet and nutritional deficiences.

. . . 5% are occupationally-related.

. . . 3% are due to radiation, largely background or natural.

. . . 2% are caused by pre-existing medical conditions such as chronic ulcerative colitis, etc.

. . . 1% is caused by prescription drugs used for the treatment of serious medical problems.

The Journal of the National Cancer Institute[6] recently published the following results of a major epidemiological study of cancer causation by Sir Richard Doll and Richard Peto of Oxford University.

Of note is the low percentage of cancer deaths attributed to occupation and the very low percentage attributed to industrial products (including man-made chemicals).

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Proportions of cancer deaths attributed to various different factors

Text section no.	Factor or class of factors	Percent of all cancer deaths: Best estimate	Percent of all cancer deaths: Range of acceptable estimates
5.1	Tobacco	30	25-40
5.2	Alcohol	3	2-4
5.3	Diet	35	1-70
5.4	Food additives	<1	-5-2
5.5	Reproductve and sexual behavior	7	1-13
5.6	**Occupation**	**4**	**2-8**
5.7	Pollution	2	<1-5
5.8	Industrial products	<1	<1-2
5.9	Medicines and medical procedures	1	0.5-3
5.10	Geophysical factors	3	2-4
5.11	Infection	10?	1-?
5.12	Unknown	?	?

These figures confirm findings of other scientific experts. Dr. John Higginson and C.S. Muir, in a study for The International Agency for Research on Cancer, estimate cancer due to occupational exposure at 2-6%; and Dr. Ernst Wynder of the American Health Foundation attributes 2-4% of cancers to occupational factors.[7,8]

What role does air or water pollution play?

Despite many scientific studies on the subject, no one has been able to demonstrate a link between general pollution and cancer.

. . . In 1959, the American Cancer Society began a study of the health patterns of a nationwide sample of one million people; in 1979, the Society reported it was unable to find a significant relationship between air pollution and cancer in this population.[9]

. . . Two other nationwide air pollution surveys, conducted by the National Cancer Institute and encompassing 20 million people, found that cancer rates were often *lower* in heavily industrialized cities than in cities with little or no heavy industry.[10,11]

. . . Dr. Higginson has reported that claims of cancer resulting from water pollution do not stand up under statistical analysis.[12]

. . . The study by Doctors Doll and Peto ranked pollution near the bottom of likely causes of cancer.[13]

Why do people assume that "environmental" cancer means "man-made" cancer?

More than a generation of massive effort to end pollution has conditioned most people to consider anything natural

as good and anything put into the environment by man as bad.

But natural substances can be dangerous too. Aflatoxin, a highly potent carcinogen, frequently is found as a natural contaminant in peanuts and other foods. Nitrosamines and estrogens, some of which are also demonstrated carcinogens, are produced in relatively significant quantities in our own bodies.

The point is that all suspect substances – natural or man-made – must be subjected to the best scientific testing possible before any conclusions are made.

Do all scientists agree with the estimate that 1-5% of cancers are due to occupational exposure?

Most scientists agree with this assessment. However, there are a few widely-known exceptions. In 1978, a widely-circulated but unpublished and unsigned report by the Department of Health, Education, and Welfare, popularly called "The Estimates Paper"[14] alleged that as much as 38% of all cancer is due to occupational exposure. These estimates are not widely accepted by the scientific community. As Dr. Doll points out, it expounds the probability that 7-10% of the 10-11 million American males exposed to asbestos *at any time, to any extent and in any manner* since the beginning of World War II, will die of mesothelioma. If this calculation is valid, then at least 10,000 mesothelioma-caused deaths should already be occurring each year. However, data from cancer registries indicate that the U.S. is experiencing less than a thousand deaths annually from mesothelioma.

Doctors Doll and Peto,[15] highly critical of the HEW paper, concluded that it "should not be regarded as a serious contribution to scientific thought" and was written "for political rather than scientific purposes."

Recently, a paper by Dr. David Hoel[16] refutes the asbestos-lung cancer conclusions rating them high by a factor of 5. The paper, which appeared in the Journal of Risk Assessment, is especially significant since Dr. Hoel was listed as a "contributor" to the original "Estimates Paper."

HEW has also predicted 7,300 lung cancer deaths a year by extrapolating from a study of smelter workers exposed to high levels of arsenic trioxide. However, these exposures occurred before occupational health protection became common to all workers who might incur any occupational exposure to arsenic in any form. As Dr. Doll[17] points out, "It follows that the population of workers that was studied epidemiologically must have been regularly exposed to concentrations of the order of 100 micrograms of arsenic trioxide dust per cubic meter of air. It is impossible to believe that the 1.5 million workers who were said to be currently exposed to arsenic could be exposed to anything like that amount."

Why would anyone over-estimate the effects of occupational exposure?

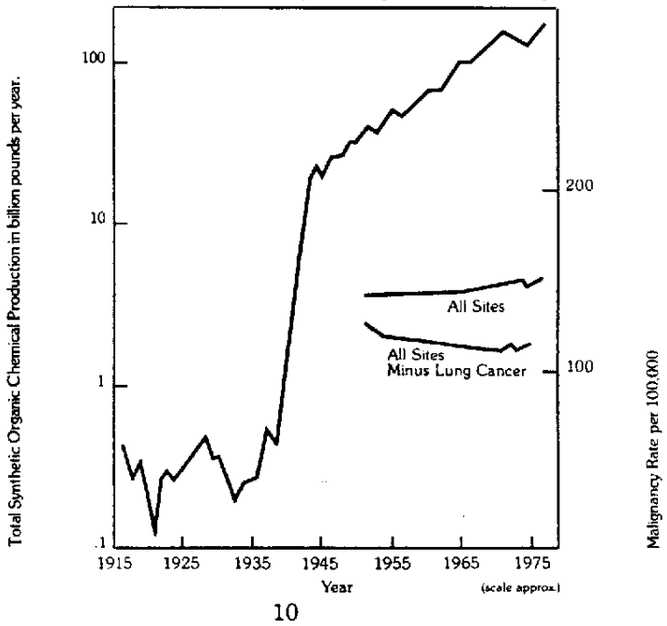
In commenting on such over-estimates, Dr. Higginson has suggested: "I don't think that some people were intentionally dishonest, but rather that they found it hard to accept that general air pollution, smoking factory chimneys, and the like are not the major causes of cancer. I mean, people would love to be able to prove that cancer is due to pollution or the general environment. It would be so easy to be able to say 'let us regulate everything to zero exposure and we have no more cancer.' The concept is so beautiful that it overwhelms a mass of facts to the contrary."[18]

How can you be so certain that the large increase in lung cancer is not related to occupational exposures?

Some cancers are clearly related to occupational exposures. But the 1-5% estimate is reasonable when considered in the light of increased chemical production over the last half century with no marked increase in cancer incidence.

Dr. W.R. Burack, writing in *Medical World News*[19] has pointed out that the age-adjusted death rates from cancer have remained nearly constant at about 140 per 100,000 population since 1935. During that same period, according to the Federal Reserve Board index, production of chemicals and allied products (and, presumably, the number of workers exposed) has skyrocketed from 29 to 810, a 28-fold increase. (See chart below).

A Comparison of the Rate of Change of Age-Adjusted Cancer Mortality Rates (average males and females, all races combined) with the Growth of the Synthetic Organic Chemical Industry



Most epidemiology studies are limited to a few hundred, or, a few thousand, individuals. However, Dr. Doll cites[20] a 16-year project conducted by the National Heart, Blood and Lung Institute among *a quarter of a million* veterans of World War II. The study showed no increase in the incidence of any cancers except those related to smoking.

The American Cancer Society study offers this conclusion: No increase in lung cancers (or cancers in other organs related to the effects of smoking) was noted among non-smokers in the population studies from 1959 to 1972. During this period, age-adjusted death rates for all Americans due to respiratory cancer more than doubled. So while occupational exposures to chemicals have been increasing, non-smoking-related cancer incidence has remained about the same or declined.

Since the effects of some carcinogens do not appear until many years after exposure, how can we be certain that a massive cancer epidemic is not in our future?

We cannot be absolutely certain that we do not face such an epidemic. However, in view of the growth of chemical production over the past 50 years, the signs of any such epidemic should already be apparent. As we have shown, no such signs have been documented by reputable scientists.

In *Carcinogens in the Workplace*, Schottenfeld and Haas[21] list a total of 34 "Industrial Agents Associated with Cancer." The latency period – the time between exposure and when cancer can be identified – most often falls between 10 and 20 years.

People who are most heavily exposed during the production of chemicals enter the workplace around age 20. So, by the time they are age 45-49, 25 to 30 years

have elapsed since their initial exposure. The death rate due to cancer in this age range (45-49) has *declined* since 1950. The American Cancer Society has also reported that there are early signs that cancer rates in the "critical 50-54 age group" are beginning to decline.[22]

Why do cancer death rates continue to increase among older people?

Primarily because deaths from all other causes have declined so dramatically. For example, deaths due to coronary heart disease declined 25% in the decade ending in 1979.[23] However, Doll and Peto[24] among others also have pointed out that diagnosis of cancer has improved substantially since 1950, particularly among older people. Sir Richard Doll has estimated that as many as half of the deaths due to cancer may have been misdiagnosed during the 1930's, particularly among older people who were less likely to have been hospitalized before death. Such errors, they suggest, have probably been reduced substantially, particularly since Medicare, introduced in 1965, increased the quality of medical care and recording of care for the aged.

Can we reduce the incidence of occupationally-related cancer below the 1-5% level?

When a cause of cancer is identified, incidence is usually reducible. For example, incidence of asbestos-related cancers has declined substantially since the introduction of protective equipment in processing plants.[25] Similar reductions have been observed among workers exposed to vinyl chloride in the manufacture of plastics.

How is industry controlling known carcinogens on the job?

Identification of a cancer-causing substance in the workplace can, and does, lead to reductions in exposure. This is often achieved by voluntary application of new technology by industry and sometimes by regulation.

While reducing or eliminating job-related exposures to carcinogens may represent a lower priority in the context of the overall cancer toll, any reduction in the occurrence of cancer among workers who may now be at risk is important to workers and management alike.

Regarding cancer, what really constitutes a "safe" working environment?

That's a very difficult question to answer.

First, experts don't agree on the criteria that should be used in labelling a substance carcinogenic.

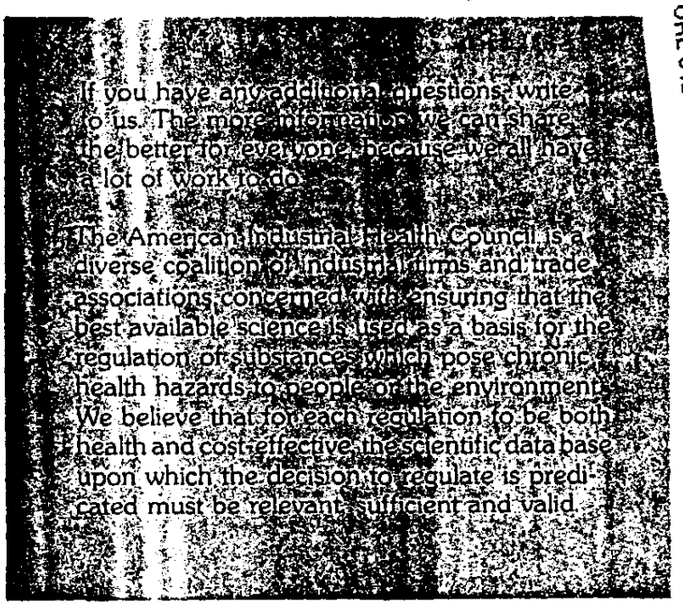
Should a compound be called carcinogenic if it causes tumors that appear to be benign? Should a chemical be regulated as a carcinogen if it causes cancer in animals exposed to doses hundreds or thousands of times greater than people would be exposed to? What percentage of experimental animals must contract what type of cancer before the evidence is sufficiently strong? Are the data from animal tests directly applicable to human situations, such as occupational exposure?

What weight should be given to emerging theories of carcinogenesis? For example, the "two-hit" theory postulates that two or more "events" are generally necessary to produce cancer. Or, the initiator/promoter theory says the effect of a chemical which initiates cancer can be tremendously magnified if followed by exposure to a "promoter" chemical; however, the promoter chemical will

not have the same effect if exposure occurs alone or prior to the initiator.

Furthermore, the latency period between exposure to a carcinogen and the appearance of cancer makes the tracing of cause and effect very difficult.

Our task, then, is to broaden our knowledge of the mechanisms of carcinogenicity, and to increase the practical applications of knowledge gained from laboratory tests. Certain tests, for example, promise to be good indicators of a carcinogen's potency, and it may become possible to extrapolate the dose-response curve from animals or animal cells to man, so that the tests become an increasingly reliable tool for establishing safe or "no-effect" levels of exposure.



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CANCER AND THE ENVIRONMENT

An Academic Review of the Environmental Determinants of Cancer Relevant to Prevention

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INTRODUCTION: DETERMINANTS OF CANCER RELEVANT TO PREVENTION, IN THE WAR ON CANCER

Joseph A. Cimino

President, New York Medical College

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We are gathered here today because we don't know all the questions, let alone the answers when it comes to environmental determinants of cancer relevant to prevention. By the end of this three-day international symposium, I hope we will have outlined one possible course and direction in this war on cancer.

1. We should be able to identify the cancer culprits that are amenable to successful intervention.
2. We must pay more attention to the factor of multiplicity and synergistic causes.
3. We must be more concerned with nutrition's role in cancer prevention.
4. We must once and for all put into their proper place the role that urban environments and occupational exposures play in the total cancer picture.
5. We must devote more energies and monies to research on life styles and know how that offers us one of our greatest prevention opportunities.
6. We must correlate intervention with the most effective cost-benefit relationships and know how to maximize the number of lives that can be saved.

Given a few minutes, most of you could easily describe numerous major cancer causing agents. As a group, I am sure that we could come up with the major culprits. I suggest that the day is here for us to say we've wasted too much time and money going after too many suspected culprits and our war on cancer is beginning to look a lot like another Viet Nam. Too much money. Too much manpower. Too much government intervention. Too much shooting in the dark. Too much waste. Too much time being devoted to snipers.

The observation from where I sit is that we have wasted a decade by concentrating on viruses and hoping to develop a miracle cure with a miracle vaccine, while letting the big cancer killers get through our front lines. Granted, significant victories have been achieved in the medical arena: improved surgical techniques, better utilization of radiation, chemotherapy, the develop-

ment of immunotherapy, and most important an aggressive and somewhat successful promotion by the American Cancer Society of the benefits of early detection.

To be objective, with Proposition 13, national health care debates and soaring medical costs, we know that cancer research money will no longer flow as freely as before. Like Viet Nam it has been a long war and we have yet to come close to achieving victory, but we can't pull out of this one. The military objective of this conference should be, and must be, to marshall our forces and attack the major culprits, give them a priority rating and go after the big ones.

In fighting the war, let us recognize the fact that it is counterproductive to use your major resources hunting down snipers. Let us spend our cancer war dollars where they will produce some significant casualities among the cancer culprits.

A personal experience that vividly illustrates some of the problems we all face in waging this war on cancer concerns the control of air pollution in New York City. It is pertinent because it focuses on the people and forces that seem to get involved: environmentalists; city, state and federal regulatory agencies; private industry; physicians; scientists; the general public and the news media.

During my tenure as Commissioner of Health of New York City, the big debate was raging over air pollution as a major cause of disease in urban America and a possible contributing factor to lung cancer. It escalated to a point where many Americans were convinced that by eliminating this "sniper," a major health hazard would disappear.

The marker chosen for control of air pollution was sulfur dioxide and although no major voice was blaming sulfur dioxide as a cancer causing agent directly, it was blamed for about everything else. At one point the citizens of New York probably believed that the City would be perfect if only SO_2 could be reduced. Hundredss of millions of dollars have been spent in New York City to burn low sulfur fuel. And I suggest to you that to this day I have yet to be convinced by any evidence that sulfur dioxide at levels reached in our urban setting is a major health hazard. Granted, on a clear day you can see the Twin Towers of the new World Trade Center but we went after SO_2 for the wrong reason. In my view the amount of money spent on this one battle may have contributed to New York City's financial plight and represents a colossal cost-benefit error.

Because of the mandatory use of low sulfur fuel, Con Edison had to convert, and the bill was paid by homeowners, renters, industry and taxpayers.

Con Ed wasn't the only victim. City facilities, of course, had to be converted as well as apartment house incinerators, which naturally raised rents.

Whether it be the campaign for cleaner air or the fight to ban saccharin, we must stop wasting money going after suspected snipers and concentrate on the major determinants of cancer. The regulation of sulfur dioxide was one of the most expensive health bullets ever fired.

The scenario on sulfur dioxide is typical of many of the same controversies over cancer causing agents and the disruptive debates now going on.

First, a regulatory agency or environmental group raises a public issue about a suspected health hazard. This is followed by some quickly gathered

scientific studies — and I use that terminology loosely — which are quoted as Gospel. Next, an activist group clamors for immediate change. The news media highlights and sensationalizes, and then we have the crisis period. Conflicting reports. Confusing counter charges. Shoddy scientific data. And finally mandated change is forced upon us, or a product is withdrawn.

I have not mentioned an important step that unfortunately is a typical flaw in our war on cancer. No one ever stops to make any real attempt to quantify the costs or effects of such a ban. It is time we apply a tourniquet to this kind of thinking and stem the flow of wasted effort and money.

If the proper effort was expended in determining the cost benefit relationship and if the best scientific data available were utilized, the conversion to low sulfur fuel in New York City would have never come about in the crisis oriented manner in which it did.

There must be objective evaluation of the risks and benefits involved and a defense against outbursts of emotionalism.

More emphasis must be placed on rational decision-making concerning the prevention of cancer.

There is little doubt that Washington continues to give the war on cancer a stamp of highest priority. However, what is most disturbing is the accusatory climate this priority has taken. Much controversy swirls around maximum tolerated levels or the pinpointing of thresholds. Things get so confusing that the EPA, OSHA, NIOSH, FDA and CPSC aren't too sure of what the other is doing. In any war, be it Viet Nam or cancer, the allies should have some idea of what each other is doing.

It may be that most of the foods we eat, the chemicals we use, the materials we manufacture will all be illegal by current or proposed Government regulations. And perhaps that's not such a bad idea, for then everyone in Washington will have to return to reality, change the ground rules and step back and take a good long look at costs and effects.

My remarks are not anti-Washington or anti-Government. Quite the contrary. We in science and education must be more aggressive in communicating with federal agencies. All too often we seem to sit back and react, usually negatively, to Government findings and regulations instead of being involved before such findings are made public policy.

I maintain that in the past many of us went along with Government to achieve our own personal and professional goals without asking a word about cost-benefit relationships. We too are to blame for some of the past sins as we strived to keep research monies flowing into our laboratories and institutions. It is time for us professionals to make the commitment that the war on cancer warrants.

The causes of cancer must be put into perspective. Normal life would not be possible if we attempted to eliminate all agents that had the potential for harm, such as Vitamins A and D, essential elements like copper and iron, sodium chloride, etc. The thought that the potentially harmful chemicals that occur naturally in food and in the air we breathe (oxygen can be toxic) are somewhat safe, while comparatively low levels of food additives or common air pollutants are dangerous, is naive.

Let us not perpetuate the tactic of going after the snipers, but rather concentrate efforts on finding out how to intervene in the major lethal cancers. Let's move viruses to a side burner and concentrate on prevention. As a physician and educator I am deeply concerned that the funds for the war on cancer continue to short-change those projects that deal with cancer prevention. We should agree that there is no absolute safety in human life and deal with the unreasonable risks to human health. Let's make a commitment that we can prevent cancer via better directed research. Let's refrain from the irresponsible misuse of cancer statistics, and agree that we have wasted millions and millions of dollars and man years in past efforts and concentrate on those areas, such as life style and diet, that can help prevent cancer now. Let's make a more objective evaluation of the risks and benefits involved and relate our efforts to the cost/benefit concept. Let's start working with, rather than against, governmental agencies. Finally, to repeat my major point, let's give prevention the major status it so richly deserves. It is not necessary to know the exact cause and pathogenesis of a disease in order to prevent its occurrence or progression. By intervening at some point in the development of a disease, at the host, vector, or agent level, we may alter its course. Examples in the history of public health are numerous: quarantines; sanitary water supplies; protection against food spoilage; the first vaccines, as against smallpox; pest and vermin control; swamp drainage; incest taboos; vitamin supplements; hypertension control.

As a result of the efforts of numerous basic scientists, clinicians and epidemiologists, we have begun to understand the major causes of cancer.

That most human cancers are caused predominantly by environmental factors is hardly disputed in present times. For the purposes of prevention, which in the long run is our most effective weapon in the War on Cancer, it is of central importance to describe what is meant by the term, environmental, since it is this term which suggests that most human cancers might be prevented or markedly delayed. An appropriate description perhaps is that given by Dr. John Higginson who helped to popularize the concept of "Environmental Cancer" starting in the 1950's:

> "...when I used the term environment in those days, I was considering the *total* environment, cultural as well as chemical. By cultural, I meant mode of life...I've checked it in every dictionary and every dictionary gives the same: Environment is what surrounds people and impinges on them. The air you breathe, the culture you live in, the agricultural habits of your community, the social-cultural habits, the social pressures, the physical chemicals with which you come in contact, the diet, and so on. A lot of confusion has arisen in later days because most people have not gone back to the early literature, but have used the word environment purely to mean chemicals" (Science, 1979).

Aside from describing what academic scientists mean when referring to the term, "Environmental Cancer", it is relevant for the purposes of launching some prevention efforts now, to identify specific predominant causes of human cancers, if at all possible. Many situations may be associated with an increased

cancer risk, but a comprehensive listing of all of these is probably not compatible with prevention because the length of such a compendium of contributing circumstances would be too long. The concept of predominant causes or factors, on the other hand, is useful for the purpose of initiating reasonable prevention efforts at the present time. The definition of a predominant cause is that in the absence of such a factor, the disease would not occur, or would be markedly less frequent. An example is smoking high-tar cigarettes and lung cancer, in both sexes, and all races. The analogy of tuberculosis and its predominant cause is also helpful in delineating the concept. In this disease, the predominant factor is the tubercle bacillus and the size of the infectious innoculum. Associated factors are crowding, malnutrition, lower socio-economic status, predisposition by diabetes mellitus or steroid therapy, inclement weather, and so on. The control of tuberculosis is most effective when aim is taken at the tubercle bacillus and the size of the innoculum; the associated societal factors must be alleviated for their own humanitarian reasons.

Any academic contributions that are made for the purposes of cancer prevention among the public must be clear cut so as not to confound individuals into apathy and inaction. Prevention messages, carried out on a massive scale, must be relatively free of confusion and therefore, the concept of specific, predominant causes has value since the potential list may be shorter than a compendium of all of the possible contributing circumstances.

The term, predominant causes, has been conceptually advanced, despite the fact that cancer is a multifactorial set of diseases. It is necessary, in order to have a high likelihood of developing cancer, to have multiple factors and circumstances operating conjointly; however, avoiding, or greatly decreasing the risk of developing cancer may only require the control of one or two predominant factors out of the whole constellation of contributing causes and circumstances.

Some of the predominant causes do fit together, such as excess use of high-tar cigarettes and heavy alcohol consumption; in such cases it is reasonable to refer to them as one set of predominant factors, especially since the two are very often used at the same time. Similarly, dietary excesses appear to constitute a constellation of sub-factors that are in co-use, and therefore comprise a second set of predominant factors that could be termed, disordered nutrition. Described in this manner, such sets of predominant factors would generally not have substantial cross-over in terms of the major types of cancers caused, and can therefore be considered, to a large extent, as separate from one another. For example, smoking high-tar cigarettes with concomitant heavy alcohol consumption constitutes one predominant cause responsible for approximately 35% of all cancer deaths in the United States (Hammond and Seidman, 1980), the cancers thought to be induced include nearly 90% of epithelial primaries in the lungs, mouth, larynx, esophagus, and liver, as well as approximately 40% of urinary bladder cancers. Disordered nutrition, which is comprised of several factors including a low-fibre diet with a high-fat intake, excess calories, plus obesity, is another predominant cause which is thought by some to account for nearly 45% of all cancer deaths in the U.S.A. (Hammond and Seidman, 1980; Upton, 1979; Nutrition and Cancer, 1977); these cancers

include between 80-90% of the epithelial primaries in the colon, rectum, breast, ovaries, and endometrium. These two categories: (1) high-tar cigarettes/alcoholism and (2) disordered nutrition may have some validity as separate, predominant causes since the types of cancers found are different. While most individuals who smoke high-tar cigarettes and drink heavily have poor nutrition, especially nutritional deficiences, their dietary patterns are not generally associated with excess calories and obesity. Most heavy smokers/drinkers have poor appetities and tend to be thin. Many of these individuals undergo major weight gains and uncontrolled appetites upon cessation of smoking and will use this to reinforce the smoking habit. The two types of lifestyles: (1) smoking and drinking to excess, and (2) eating to excess with a predominant high-fat, low-fibre diet, seem to be somewhat segregated and are associated with different types of cancers. This is undoubtedly an over-simplification, especially since heavy smokers/drinkers tend to be malnourished, and therefore also have "disordered nutrition"; however, this is of a different type from the disordered nutrition that is linked to the causation of cancers of colon, rectum, breast, ovaries, and endometrium.

The area of nutritional deficiences is probably applicable to both types of predominant causes discussed so far, i.e., (1) excess smoking/drinking and (2) low-fibre diet with excess calories/fat ingestion/obesity. Deficiences of vitamin A, other retinoids, antioxidants, selenium etc. can occur as a result of poor appetites, as occurs in heavy smokers/drinkers, or as a result of consuming excess quantities of only a few types of foods. Obese individuals can and often do have nutritional deficiences, especially of antioxidants. At a symposium sponsored by the American Health Foundation, in 1979, a group of medical scientists concurred that the dramatic decline in stomach cancers, from the major lethal cancer to its present comparative rareness, is due largely to the greater availability of low-cost, fresh produce, made available by an efficient infrastructure of rapid trucking and refrigerated freight carriers; the net result being the greater consumption of more varied, fresh produce with, presumably, enhanced intake of different trace nutrients and antioxidants (Preventive Medicine, Vol. 9, 1980).

The value of attempting to segregate the predominant causes, and the types of related cancers, centers on the effectiveness of prevention-education and, to some extent, targeted early detection programs. Public health messages must be clear and specific. If predominant causes can be identified, in general, with specific types of major, lethal cancers, then public education for prevention and targeted early detection will be easier. The overall purpose in trying to simplify the predominant causes of cancer is to inititate prevention education now. As further research is performed to verify the major causes of cancer, new and more appropriate public health education can be developed.

Several symposia (Nutrition and Cancer, 1977; Preventive Medicine, Vol. 9, 1980) and individuals like J. Higginson (Science, 1979) and A. Upton (Upton, 1979) have developed relatively short lists of specific predominant causes, quite independently of one another. The concordance among these observers is good; Table 1 reproduces these with a relative percent contribu-

TABLE 1. Predominant Sets of Factors in Developing Cancer**

Estimated Relative Percentage	Approximate Number of Such Cancer Deaths*
• 35% of cancer deaths are predominantly due to smoking high-tar cigarettes and consuming excess amounts of distilled liquor (this includes 90% of the cancers of the lungs, mouth, larynx, esophagus and liver, plus 40% of cancers of the urinary bladder)	350 cancer deaths per day
• 45% are predominantly caused by disordered nutrition, with the following subcategories: a) excess calories b) excess fat ingestion, including saturated and unsaturated fats, as well as cholesterol c) obesity, of a magnitude of 40 lbs. or more overweight, for the average individual d) nutritional deficiencies, especially dietary fiber and retinoids (the latter includes vitamin A deficiency; however, only the recommended daily allowance is needed; excesses are extremely dangerous) (the cancers that relate to disordered nutrition are most of the cancers of the colon, rectum, stomach, breast, and many of the cancers of the ovaries and endometrium)	450 cancer deaths per day
• 5% or less of the present deaths are due predominantly to occupational exposures that occurred in the past when the dangers were not known (the cancers that are generally included represent a small proportion of the malignancies of the urinary bladder, lung, nasopharynx, stomach, hemolymphatic system, liver, bones and skin)	50 cancer deaths per day
• 3% are predominantly due to ionizing radiation; about ⅔ of these are due to "background", or naturally occurring radiation, and ⅓ to medical radiation	30 cancer deaths per day
• 2% are due predominantly to pre-existing, benign medical disorders such as chronic fibrocystic disease of the breast, ulcerative colitis, regional enteritis, and chronic atrophic gastritis	20 cancer deaths per day
• 1% are due predominantly to the administration of prescribed pharmaceutical agents such as cancer chemotherapeutics, estrogens for the menopause, and possibly some anti-hypertensive drugs	10 cancer deaths per day

*Approximately 1,000 individuals in the United States die every day from cancer, i.e., about 365,000/year.
**(Editor's Inverview, 1979; Hammond and Seidman, 1980; Upton, 1979; Wynder, 1980).

tion, in a highly tentative manner. These percentages represent working figures and are only estimates to be probed and tested through further research.

Since these sets of predominant causes in Table 1 are largely segregated, it is valid to add them separately to develop an idea of approximately how much of the cancer burden might be preventable, or put off to a later time in life. It is fair to say that the preponderant causes of most of the lethal cancers in the U.S.A. are known, and present varying degrees of difficulty in terms of public health education. A comparatively small relative percent of cancers have unknown predominant causes, about 10%.

While public health education in cancer prevention requires clarity and simplification, academic standards require full and more complex considerations. Therefore, tabular estimates of the relative percent contribution by various predominant causes have limited academic value and must be modulated by some scientific input in order to avoid mistaken simplifications. For example, while low-fibre diets are thought to be a major factor in the development of colon/rectal cancer, the simplistic corollary that indiscriminate high-fibre intakes would offer prevention requires an answer to the question of "...what type of fiber?". It is entirely possible to experimentally enhance mucosal contact with carcinogens adsorbed on certain types of fibres. Rather than focusing on one aspect of disordered nutrition, it would be perhaps more relevant to realize that low-fibre diets are generally also high fat and lack sufficient fresh produce. The fibre content relates to enteric transit time, and possible also to the adsorptive capacity of the fibre. Transit time may be important since it may affect the duration of exposure of the mucosal epithelium to enteric carcinogens and "promoters"; however, copious fluid intake, high carbohydrate diets and physical activity can also decrease enteric transit time. Therefore, it is possible to see how lifestyle and diet interface and why the term disordered nutrition is a constellation of factors that includes obesity, with its presumed relative inactivity, together with excess calories, high fat intake and low fibre.

Against this type of background, a number of academicians decided that the complexities involved in the development of the major lethal cancers had to be presented to the relevant segments of society, and to the public at large through the media. The Cancer Symposium was under the co-sponsorship of the New York Academy of Sciences and the Cancer Symposium Committee, and was held in cooperation with the American Cancer Society. The Speakers and Chairpersons were selected by the Cancer Symposium Committee and reviewed by the New York Academy of Sciences and the American Cancer Society. These Speakers and Chairpersons reported on work that was supported by peer-reviewed grants/contracts from the N.I.H., N.S.F., W.H.O., the American Cancer Society, the National Research Council, and granting sources in several countries.

The Cancer Symposium was organized into sequential sessions that attempted to answer the following questions:

- How do chemical/physical agents in the personal and general environment cause normal cells to become cancer cells?
- Are there clues in existing human data that can direct the basic

researchers to the causes of cancer? For example, are there groups of people who follow particular lifestyles that either predispose, or protect them? Are there areas of our country where cancer rates are particularly high, and if so are there consistent factors when scientific controls are studied?

- What are the causes of the lethal cancers, as shown by human epidemiology and animal experiments?
- What are the contributions of high-tar versus low-tar cigarettes, excessive alcohol consumption, general pollution, disordered nutrition, nitrites/nitrates, saccharin/cyclamate, administration of pharmaceuticalsubstances?
- Are there ways to scientifically extrapolate data, since there is a real need to protect workers, communities and consumers right now? Are there systems available now that can be logically used to help determine risk?
- If exposures have occured, is it possible to intercede during the well-known lag phase (between exposures and development of cancer) with chemicals that might act as "antidotes"? For example, can anything be done to prevent the progression of asbestos-related diseases among the individuals who were exposed 15-30 years ago, at a time when the dangers of heavy exposures were not clear?

The presentations did provide significant portions of the answers to the above questions and additionally offered data on the following points which are discussed and summarized following the Conference Conclusions; these include the questions:

- Is there a cancer epidemic involving most anatomic sites, or is it just lung cancer that is epidemic?
- Is there a reasonable biologic basis for practical thresholds to many of the predominant causes of cancer?
- Is synergism a significant factor, since most humans have multiple exposures? Is there a way of approching this question on a practical basis?
- Is it likely that industrial and general pollution of air and water will lead to major increases in cancer rates (per 100,000) in the future, in view of increases in industrial production and in population?
- What are the percent relative contributions of widely publicized factors such as general community air pollution, general water pollution and saccharin/cyclamates?

ACKNOWLEDGEMENTS

It is imperative to understand that the advances in the War on Cancer have come about by the concerted efforts of basic scientists, clinicians, biostatisticians, epidemiologists, lay lobbyists, legislators, and administrators in many parts of the world. It is hoped that their efforts will continue, particularly